

SEQUENCE LISTING

<110> Sprecher, Cindy A.
Kisiel, Walter
Foster, Donald C.

<120> NOVEL HUMAN KUNITZ-TYPE INHIBITORS AND
METHODS RELATING THERETO

<130> 93-14D4

<150> US 09/904,621
<151> 2001-07-13

<150> US 09/265,627
<151> 1999-03-09

<150> US 08/457,887
<151> 1995-06-01

<150> US 08/147,710
<151> 1993-11-05

<160> 15

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<211> 979
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (39)...(746)

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Met Asp Pro Ala Arg Pro
1 5

ctg ggg ctg tcg att ctg ctg ctt ttc ctg acg gag gct gca ctg ggc 104
Leu Gly Leu Ser Ile Leu Leu Leu Phe Leu Thr Glu Ala Ala Leu Gly
10 15 20

gat gct gct cag gag cca aca gga aat aac gcg gag atc tgt ctc ctg 152
Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn Ala Glu Ile Cys Leu Leu
25 30 35

ccc cta gac tac gga ccc tgc cgg gcc cta ctt ctc cgt tac tac tac 200
Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu Leu Arg Tyr Tyr Tyr
40 45 50

gac agg tac acg cag agc tgc cgc cag ttc ctg tac ggg ggc tgc gag 248
Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe Leu Tyr Gly Gly Cys Glu
55 60 65 70

ggc aac gcc aac aat ttc tac acc tgg gag gct tgc gac gat gct tgc 296
Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu Ala Cys Asp Asp Ala Cys
75 80 85

tgg agg ata gaa aaa gtt ccc aaa gtt tgc cgg ctg caa gtg agt gtg	344
Trp Arg Ile Glu Lys Val Pro Lys Val Cys Arg Leu Gln Val Ser Val	
90 95 100	
gac gac cag tgt gag ggg tcc aca gaa aag tat ttc ttt aat cta agt	392
Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys Tyr Phe Phe Asn Leu Ser	
105 110 115	
tcc atg aca tgt gaa aaa ttc ttt tcc ggt ggg tgt cac cgg aac cgg	440
Ser Met Thr Cys Glu Lys Phe Phe Ser Gly Gly Cys His Arg Asn Arg	
120 125 130	
att gag aac agg ttt cca gat gaa gct act tgt atg ggc ttc tgc gca	488
Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr Cys Met Gly Phe Cys Ala	
135 140 145 150	
cca aag aaa att cca tca ttt tgc tac agt cca aaa gat gag gga ctg	536
Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser Pro Lys Asp Glu Gly Leu	
155 160 165	
tgc tct gcc aat gtg act cgc tat tat ttt aat cca aga tac aga acc	584
Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe Asn Pro Arg Tyr Arg Thr	
170 175 180	
tgt gat gct ttc acc tat act ggc tgt gga ggg aat gac aat aac ttt	632
Cys Asp Ala Phe Thr Tyr Thr Gly Cys Gly Gly Asn Asp Asn Asn Phe	
185 190 195	
gtt agc agg gag gat tgc aaa cgt gca tgt gca aaa gct ttg aaa aag	680
Val Ser Arg Glu Asp Cys Lys Arg Ala Cys Ala Lys Ala Leu Lys Lys	
200 205 210	
aaa aag aag atg cca aag ctt cgc ttt gcc agt aga atc cgg aaa att	728
Lys Lys Lys Met Pro Lys Leu Arg Phe Ala Ser Arg Ile Arg Lys Ile	
215 220 225 230	
cgg aag aag caa ttt taa acattcttaa tatgtcatct tgtttgtctt	776
Arg Lys Lys Gln Phe *	
235	
tatggcttat ttgcctttat ggttgtatct gaagaataat atgacagcat gaggaaacaa	836
atcattggtg atttattcac cagttttat taataacaat cacttttca aaaatttgaa	896
ttttttataataacttagc tgctattcaa atgtgagtct accattttta atttatggtt	956
caactgttttg tgagactgaa ttc	979
<210> 2	
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Met Asp Pro Ala Arg Pro Leu Gly Leu Ser Ile Leu Leu Leu Phe Leu	
1 5 10 15	
Thr Glu Ala Ala Leu Gly Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn	
20 25 30	
Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu	
35 40 45	
Leu Leu Arg Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe	
50 55 60	
Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu	
65 70 75 80	
Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys	

85	90	95
Arg Leu Gln Val Ser Val Asp Asp Gln	Cys Glu Gly Ser Thr Glu Lys	
100	105	110
Tyr Phe Phe Asn Leu Ser Ser Met	Thr Cys Glu Lys Phe Phe Ser Gly	
115	120	125
Gly Cys His Arg Asn Arg Ile	Glu Asn Arg Phe Pro Asp Glu Ala Thr	
130	135	140
Cys Met Gly Phe Cys Ala Pro Lys Lys	Ile Pro Ser Phe Cys Tyr Ser	
145	150	160
Pro Lys Asp Glu Gly Leu Cys Ser Ala	Asn Val Thr Arg Tyr Tyr Phe	
165	170	175
Asn Pro Arg Tyr Arg Thr Cys Asp Ala	Phe Thr Tyr Thr Gly Cys Gly	
180	185	190
Gly Asn Asp Asn Asn Phe Val Ser	Arg Glu Asp Cys Lys Arg Ala Cys	
195	200	205
Ala Lys Ala Leu Lys Lys Lys	Lys Met Pro Lys Leu Arg Phe Ala	
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Ser Arg Ile Arg Lys Ile Arg Lys Lys	Gln Phe	
225	230	235

<210> 3
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<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide ZC4792

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30

<210> 4
<211> 30
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<213> Artificial Sequence

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<223> Oligonucleotide ZC6281

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<210> 5
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Clone M-2161

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38

<210> 6
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> M-2177

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<400> 6
gaaacctcta gacttatatac ctccagcaag catc 34

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<222> (77)...(235)

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ataaacgacc aaaaga atg aag gct gtt ttc ttg gtt ttg tcc ttg atc gga 112
Met Lys Ala Val Phe Leu Val Leu Ser Leu Ile Gly
1 5 10

ttc tgc tgg gcc caa cca gtc act ggc gat gaa tca tct gtt gag att 160
Phe Cys Trp Ala Gln Pro Val Thr Gly Asp Glu Ser Ser Val Glu Ile
15 20 25

ccg gaa gag tct ctg atc atc gct gaa aac acc act ttg gct aac gtc 208
Pro Glu Glu Ser Leu Ile Ala Glu Asn Thr Thr Leu Ala Asn Val
30 35 40

gcc atg gct gag aga ttg gag aag aga 235
Ala Met Ala Glu Arg Leu Glu Lys Arg
45 50

<210> 8
<211> 53
<212> PRT
<213> Homo sapiens

<400> 8
Met Lys Ala Val Phe Leu Val Leu Ser Leu Ile Gly Phe Cys Trp Ala
1 5 10 15
Gln Pro Val Thr Gly Asp Glu Ser Ser Val Glu Ile Pro Glu Glu Ser
20 25 30
Leu Ile Ile Ala Glu Asn Thr Thr Leu Ala Asn Val Ala Met Ala Glu
35 40 45
Arg Leu Glu Lys Arg
50

<210> 9
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Nor-1478

<400> 9
gtaaaacgac ggccagt 17

<210> 10
<211> 21
<212> DNA
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<220>
<223> NOR-2523

<400> 10
tctttctcc aatctctcag c 21

<210> 11
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> M-2162

<400> 11
cttttactct agacttactt tggtgcgca g aagcc 35

<210> 12
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal

<400> 12
Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn
1 5 10

<210> 13
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal

<400> 13
Ala Gln Glu Pro Thr Gly Asn Asn
1 5

<210> 14
<211> 165
<212> DNA
<213> Artificial Sequence

<220>
<221> variation
<222> (0)...(0)
<223> Kunitz domain

<221> variation
<222> (1)...(3)
<223> Codon-1 Wherein the nucleotide triplet 1-3
      encodes any amino acid except cysteine.

<221> variation
<222> (4)...(6)
<223> Codon-2 Wherein the nucleotide triplet 4-6

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encodes any amino acid except cysteine.

<221> variation
 <222> (160)...(162)
 <223> Codon-54 Wherein the nucleotide triplet 160-162
 encodes any amino acid except cysteine.

<221> variation
 <222> (163)...(165)
 <223> Codon-55 Wherein the nucleotide triplet 163-165
 encodes any amino acid except cysteine.

<400> 14
 nnnnnnntgtc tcctgccccct agactacgga ccctgccggg ccctacttct ccgttactac 60
 tacgacaggt acacgcagag ctgccgcag ttccctgtacg ggggctgcga gggcaacgcc 120
 aacaatttct acacctggga ggcttgcac gatgcttgcn nnnnn 165

<210> 15
 <211> 55
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Kunitz Domain

<221> VARIANT
 <222> (1)...(2)
 <223> aal-2 Wherein each amino acid from position 1 to
 2 is individually any amino acid except cysteine.

<221> VARIANT
 <222> (54)...(55)
 <223> aa54-55 Wherein each amino acid from position 54
 to 55 is individually any amino acid except
 cysteine.

<400> 15
 Xaa Xaa Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu Leu
 1 5 10 15
 Leu Arg Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe Leu
 20 25 30
 Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu Ala
 35 40 45
 Cys Asp Asp Ala Cys Xaa Xaa
 50 55